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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,592	08/02/2001	Ingvar Mats Ferby	100564-00064	2983

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EXAMINER
SNEDDEN, SHERIDAN

ART UNIT	PAPER NUMBER
1653	9

DATE MAILED: 01/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,592	FERBY ET AL.	
	Examiner	Art Unit	
	Sheridan K Snedden	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)[·] Responsive to communication(s) filed on *24 October 2002* .

2a)[ ] This action is **FINAL**. 2b)[X] This action is non-final.

3)[ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)[·] Claim(s) *1-16 are cancelled and claims 17-36* is/are pending in the application.

4a) Of the above claim(s) *21-32 and 34-36* is/are withdrawn from consideration.

5)[ ] Claim(s) _____ is/are allowed.

6)[·] Claim(s) *17-20 and 33* is/are rejected.

7)[ ] Claim(s) _____ is/are objected to.

8)[ ] Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)[ ] The specification is objected to by the Examiner.

10)[·] The drawing(s) filed on *02 August 2001* is/are: a)[ ] accepted or b)[X] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)[ ] The proposed drawing correction filed on _____ is: a)[ ] approved b)[ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)[ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)[·] Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)[X] All b)[ ] Some * c)[ ] None of:

1.[X] Certified copies of the priority documents have been received.

2.[ ] Certified copies of the priority documents have been received in Application No. _____ .

3.[ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)[ ] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) [ ] The translation of the foreign language provisional application has been received.

15)[·] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [·] Notice of References Cited (PTO-892)
2) [·] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [·] Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6*
4) [ ] Interview Summary (PTO-413) Paper No(s). _____ .
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other

DETAILED ACTION

1. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not). Applicant's response filed October 24, 2002 cancels claims 1-17 and adds new claims 18-37, which appears to be in error as the application as filed contains claims 1-16. Therefore claims 1-16 have been cancelled and misnumbered new claim 18-37 have been renumbered 17-36.Applicant's state that a typographical error in the preliminary Amendment dated August 8, 2002 incorrectly numbers the claims being amended. No such error can be found in the Amendment as amended claims 3 and 4 correspond correctly with the original claims as filed. Therefore, the claims have been renumbered as stated above. To eliminate further confusion, cancelled claims 17-18 and 20-33 are considered to have the same scope and correspond to claims 1-16 originally filed as indicated by the table below.

Claim	1	corresponds to Claim	17, 18
Claim	2	corresponds to Claim	19
Claim	3	corresponds to Claim	20
Claim	4	corresponds to Claim	21
Claim	5	corresponds to Claim	22
Claim	6	corresponds to Claim	23
Claim	7	corresponds to Claim	24
Claim	8	corresponds to Claim	25
Claim	9	corresponds to Claim	26
Claim	10	corresponds to Claim	27
Claim	11	corresponds to Claim	28
Claim	12	corresponds to Claim	29
Claim	13	corresponds to Claim	30
Claim	14	corresponds to Claim	31
Claim	15	corresponds to Claim	32

Claim 16 corresponds to Claim 33

3. Therefore, Applicant's cancellation of claims 1-16 and addition of new claims 17-36 is acknowledged. Applicant's election of invention I, claims 17-20 and 33, drawn to DNA and expression vector is acknowledged. Claims 34-36 are newly added in Paper No. 8, filed October 12, 2002 and are outside the scope of the elected invention. Claims 1-16 are cancelled and claims 21-32 and 34-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8. Claims 17-20 and 33 are under examination.

Drawings

4. The drawings are objected to for the reasons indicated on the accompanying form PTO 948. Corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. See 37 CFR 1.85(a) and MPEP 608.02(b).

Claim Objections

Claim 17 objected to because of the following informalities: The claim in (a) recites a sequence "a sequence as shown in SEQ ID NO: 1 or 2". As the sequences are not displayed by the claim, it is suggested that the language be changed to "a sequence of SEQ ID NO: 1 or 2".

Claim Rejections - 35 USC § 101

5. Claims 17-19 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. As stated, the claims recite a peptide of natural origin and do not

show the hand of man. Applicant is advised to include the words "isolated" or "purified" in the recitation of the invention directed towards protein to indicate the hand of man.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 17-20 and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA sequence of SEQ ID NO: 1 and DNA encoding the protein of SEQ ID NO: 2, does not reasonably provide enablement for all sequences that would hybridize to the above sequences or all genomic sequences from all species for the above sequences. Furthermore, the specification does not does not reasonably provide enablement for all genomic sequences from all species for the sequence of SEQ ID NO: 1. The specification does not give any guidance as to the full range of all existing sequences that could hybridize to the DNA sequences above or to all genomic sequences for all species of SEQ ID NO: 1 as recited in the instant claims. In In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the breadth of the claims,
3. the state of the prior art,
4. the predictability or lack thereof in the art,
5. the amount of direction or guidance present,
6. the presence or absence of working examples,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

1) the nature of the invention;

In the instant case, Applicants are claiming a DNA sequence (SEQ ID NO: 1) encoding a protein (SEQ ID NO: 2) that may be used for inducing oocyte maturation or modulating cell proliferation.

2) the breadth of the claims;

As recited in claim 17(c), the breadth of the claim is directed to all sequences that would hybridize to SEQ ID NO: 1 or a DNA encoding the protein of SEQ ID NO: 2.

As recited in claim 17(d) and 17(e), the breadth of the claim is directed to all cDNA sequences and all genomic sequences which encode for a protein homologs of the protein of SEQ ID NO: 2. All such proteins would have the capability to induce oocyte maturation or modulate cell proliferation.

3) the state of the prior art; and,

DNA hybridization techniques are routine procedures in the art and may be optimized by altering the parameters of salt and detergent concentration, time and temperature.

The sequences of SEQ ID NO: 1 or 2 are not described in the art. Additionally, no apparent homologs or genomic sequences to the DNA and protein of SEQ ID NO: 1 and 2 are identified by a search of the art. Therefore, these is no guidance present in the prior art as the conditions of hybridization to be used using the DNA sequence of SEQ ID NO: 1.

4) the amount of direction or guidance presented;

5) the presence or absence of working examples;

The specification and claims fail to define stringent conditions. On page 3, the specification mentions that the conditions for hybridization are stringent but fail to provide clear instruction as to the parameters of salt and detergent concentration, time and temperature. None of the examples provided in the specification define the conditions of hybridization that are to be read in the claim.

The instant specification does not give any guidance to the genomic sequence containing SEQ ID NO 1. Page 2 of the specification teaches that cDNA was prepared and cloned into expression vectors. Example 1-4 teaches the preparation and use of a cDNA library. The specification fails to provide any discussion as to the genomic sequence, such as identification of introns and exons or position of the gene on the chromosome.

Likewise, there is no guidance for identifying sequences from all species, such as what sequence elements, domains, and biological function are critical that would define a family of sequences.

6) the predictability or unpredictability of the art;

DNA hybridization techniques may be used for quantification of a specific DNA or may be used to search sequences of like sequence identity. The determinants of hybridization are the percent identity of the hybridizing DNA molecules and the parameters discussed above. However, without specific conditions of hybridization, the results are unpredictable. For instance, Ishibashi *et al.* teach a cDNA that shares a sequence identity of 60.7% between nucleotides 381 and 902 of SEQ ID NO: 1. The cDNA taught be Ishibashi *et al.* would not have similar biological activity as the DNA sequence claimed in the present invention. Thus, not all sequences that would hybridize to SEQ ID NO: 1 would have the same function used for inducing oocyte maturation or modulating cell proliferation. The person of skill in the art would not be able to identify sequences used for inducing oocyte maturation or modulating cell proliferation with any predictability given the direction provided by the specification. Furthermore, the identification of all genomic sequences from all species for all sequences which hybridize to the sequence of SEQ ID NO: 1 would also be unpredictable.

The genomic sequence of SEQ ID NO: 1 and genomic sequences from all species are likewise unpredictable. There is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, and therefore, the result are unpredictable. There is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

7) the quantity of experimentation necessary;

The courts have interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). As such, the quality of experimentation necessary to identify and qualify all sequences that hybridize to the SEQ ID NO: 1 under undefined conditions is undue.

8) the relative skill of those skilled in the art;

In view of the discussion of each of the preceding seven factors the level of skill in this art is high and is at least that of a PhD or a person with several years of experience in the art. As

the cited art would point to, even with a level of skill in the art which is high, predictability of the results is not invariable.

In consideration of each of factors 1 – 8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching, and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-20 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17, and dependent claims thereto, recite "a DNA sequence" of SEQ ID NO: 2, however, SEQ ID NO: 2 is an amino acid sequence and not a DNA sequence. Thus, the claim is indefinite.

The term "stringent" in claim 17(e) is a relative term which renders the claim indefinite. The term "stringent" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of "stringent".

Claim 17(e) is indefinite because it is unclear as to what sequence differences would be due to its origin from a different species. What number of sequence changes are allowable to maintain the same biological function, and when does the sequence become an isoform or

another entity altogether? Note also that "capable of" does not equate to must invariably occur; and, thus the claims are indefinite as indicating only a potential function/action.

Claims 33 is indefinite because it is unclear as to which part of the sequence may be used as a diagnostic marker. Is a single base from the DNA sequence considered a part of the sequence that may be used as a diagnostic marker?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 17-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Reddy *et al.* (US Patent 4,923,805). Reddy *et al.* teach human FSH which differs in origin from the Xenopus DNA sequence of SEQ ID NO: 1 or 2 as recited in claim 17(e). Reddy *et al.* teach follicle stimulating hormone (FSH) which possesses the biological function of modulating cell division as a promoter of estrogen synthesis and follicle cell growth (regarding claim 18). Reddy *et al.* teach the production of FSH using an expression vector that contains expression control sequences (regarding claims 19 and 20). Thus, the reference anticipates the claimed invention.

9. Claims 17 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Sager *et al.* (US Patent 4,923,805). Sager *et al.* describes the process of subtractive hybridization as a general method for recovering genes that are expressed in normal cells but not in closely related

tumor cells. Sager *et al.* further describes the isolation of three clones by subtractive hybridization of normal and cancerous mammary cells. The genes corresponding to these clones are expressed by all normal mammary epithelial cells, but not by any primary mammary tumors or mammary tumor cell lines. One such gene encodes keratin 5, which is said to be a valuable marker to distinguish normal and primary tumor cells in culture. Keratin 5 differs in origin from the Xenopus DNA sequences of SEQ ID NO: 1 or 2. Thus, the reference anticipates the claimed invention.

Conclusion

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan K Snedden whose telephone number is (703) 305-4843. The examiner can normally be reached on Monday - Friday, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone number for regular communications to the organization where this application or proceeding is assigned is (703) 746-3975.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Christopher S. Low

SKS
January 26, 2003

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